REMARKS/ARGUMENTS

Applicants respond to the Examiner's comments using the paragraph of the office action. Support for the amendment to claim 87 is provided at p. 35, lines 10-11. The recitation of "and/or" in the first line of the monitoring step of claim 87 is consistent with the parallel use of this term elsewhere in this step, and does not raise new issues. New claims 99 and 100 have been added. Support for new claims 99 and 100 is provided at, *e.g.*, p. 34, lines 1-7.

5. Claims 50, 69-70, 73-86 and 90-08 stand withdrawn from consideration as being directed to a nonelected invention. The Examiner alleges that claims 50, 69-70, 73-80 and 89 (drawn to clearing tissue samples), claims 81-86 (drawn to clearing isolated biological entities), and claims 90-97 (drawn to clearing amyloid deposits) are distinct in recitation as to the previous claims. Applicants respectively traverse.

The amendment to claim 50 in the last response does not change the nature of the claim such as to place it outside the elected restriction group. In brief, applicants amended the preamble from "biological entity physically associated with an antigen" to a "tissue sample," and made parallel amendments to the rest of the claim for conformity with the preamble. A tissue sample is a species of biological entity associated with an antigen (see specification at p. 34, lines 25-26). The amended claim thus focuses the scope of the biological entity on which the antibody is to be screened but does not otherwise change the nature of the method. The amended claim remains within the scope of the original claim and would have been included within any search that was done on the previous claim. Further, the amendment was made to address the Examiner's allegation that the preamble of claim 50 (before the amendment) was inconsistent with the body of the claim (see office action of December 11, 2002 at p. 5-6). It is not understood how a focusing amendment responsive to specific comments in the office action can be seen as placing a claim outside the elected group.

Moreover, it is noted that the elected group was actually characterized by the Examiner as drawn to a "method of screening with a cell" (restriction requirement of March 12, 2002 at p. 2). As explained in the previous response, a tissue sample comprises an aggregation of similarly specialized cells united in performing a particular function." Thus, a method of

screening a tissue sample (as specified in amended claim 50) falls within this group at least as much as a biological entity physically associated with an antigen , which may, but need not be a cell (as specified in original claim 50).

The remaining independent claims designated in the office action as distinct Groups are also species of original claim 50. Claim 81 is directed to screening an antibody against an isolated biological entity (another example of a biological entity physically associated with an antigen). Claim 87 is directed to screening a biological entity physically associated with an antigen, where the entity is a tissue sample selected from a defined group. Similarly, an amyloid deposit as recited in claim 90 is a further example of a biologically entity physically associated with an antigen. Given that the independent claims now pending represent species of the originally elected independent claim, it is submitted that they should have been at most be subject to an election of species rather than to a restriction requirement. In this event, applicants would have elected to pursue claim 50 and dependent claims.

For the reasons discussed above, it is submitted that amended claim 50 (and dependent claims) remains within the elected group and should be the subject of further prosecution. Because the Examiner has already examined claim 87, and its subject matter is closely related to claim 50 (both claims are directed to method of screening an antibody for activity in clearing a tissue sample), it is suggested that this claim remain under prosecution.

7. Claims 87-89 stand rejected under 35 USC 102(b) as anticipated by Jorbeck. Jorbeck is said to teach in vitro assays involving combination of PEC exudates containing phagocytic cells bearing Fc receptors with serum containing antibodies, Salmonella (an antigen/biological entity) and monitoring clearance of Salmonella. The Examiner says that PEC exudates are aggregates of specialized cells that perform the lytic function. Applicants maintain the traverse.

As Applicants understand the rejection, the Examiner is alleging that Jorbeck's PEC exudates provide both the tissue and phagocytic cells of the present claims, and that the Salmonella in Jorbeck provides the antigen of the present claims. If so, Jorbeck fails to anticipate for two reasons. First, if the PEC exudates serve both as a tissue sample and a source of phagocytic cells, Jorbeck does not satisfy the claim requirement of *combining* a tissue sample

with phagocytic cells. Under the Examiner's interpretation of Jorbeck, the tissue sample and phagocytic cells are one and the same, and cannot be brought together in a combining step. Second, Jorbeck's antigen is not physically associated with Jorbeck's tissue. The antigens on Salmonella are physically associated with Salmonella but not the PEC exudates (which constitute the tissue under the Examiner's interpretation of Jorbeck). For these reasons, withdrawal of the rejection is respectfully requested.

8. Claims 87-89 stand rejected under 35 USC 102(e) as anticipated by Vitek for reasons of record. In the previous response, applicants pointed out that Vitek's method differs from that claimed in at least two respects: (1) Vitek does not disclose simultaneous presence of an antibody and phagocytic cells in an *in vitro* clearing reaction: and, (2) nor does it disclose that the clearing reaction screens an antibody for clearing activity. The Examiner now says that Vitek discloses suitable assays for *in vitro* analysis of target agents that promote the clearance of amyloid plaques, and that the reference includes where the agents are antibodies, and tissues samples use phagocytic cells. The Examiner alleges that although Vitek references a particular assay with thioflavin, the reference teachings are not limited to this particular assay, and that assay does not negate cumulative teachings as to assays to detect clearance of plaques. Traverse is respectively maintained.

Although Vitek discusses various methods of treatment and diagnosis, only a small portion of the patent relates to an *in vitro* assay for phagocytosis at col. 22, lines 54-66. As discussed in the last response and reiterated below, the assay discussed at col. 22, lines 54-66 is not the same as that claimed. In Vitek's *in vitro* assay, the object is not to screen an antibody but rather to screen AGE -TF (thioflavin) for capacity to modify insoluble or aggregated Aβ (col. 22, lines 53-55). This is achieved by the following steps. First, AGE-TF is contacted with aggregated Aβ. The incorporation of AGE-TF into aggregated Aβ is then tested by ELISA using an antibody (col. 22, lines 58-61). The antibody in this step is used simply as a conventional diagnostic reagent, and is not itself being screened for anything. After verifying incorporation of AGE-TF, phagocytic cells are added to test for clearance of AGE-TF modified Aβ (col. 22, lines 61-65). However, at the time the phagocytic cells are added, there is no indication that the antibody used for the ELISA is still present. It would be most logical and typical practice when

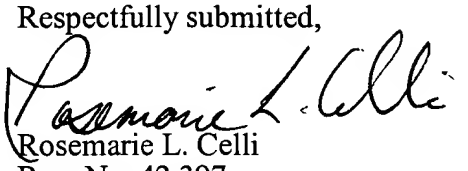
performing a diagnostic step on an intermediate product in a process to perform the diagnostic step on only a sample of the intermediate so as to avoid influencing the further processing of the intermediate by contamination with the reagents in the diagnostic step. In any event, insofar as there is doubt as to whether Vitek proposes adding phagocytic cells to the same or a different vessel to that in which the ELISA using antibody to AGE-TF is performed, that doubt should inure to the benefit of applicants given that the burden of proof rests on the PTO (*In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984)).

The Examiner's comment that Vitek's assay is not limited to an ELISA of thioflavin misses the point of the above analysis. The point is not that Vitek discusses only an ELISA of thioflavin but rather that Vitek does not disclose that the antibody used in this ELISA is present in the phagocytic assay discussed subsequently. The Examiner also generally points to "cumulative teachings" of Vitek as suggesting modification of the phagocytic assay actually disclosed by Vitek. However, the Examiner does not identify with particularity which teachings she is referring to nor how they suggest modification of the actual phagocytic assay used by Vitek. Although it is undisputed that Vitek discusses a number of subjects regarding the role of AGE's in amyloidogenic disease, and potential treatment of the same, it is not apparent how any of them relate to an in vitro method of screening antibodies for phagocytosis. In particular, it is not apparent how any other disclosure in Vitek would lead one to alter Vitek's actual in vitro phagocytosis assay by including an antibody to be screened in the assay.

If the rejection is maintained, applicants request the Examiner to identify with particularity, the basis, if any, for her disagreement with applicants' explanation of Vitek's phagocytosis assay discussed at col. 22, lines 61-65, and to identify with particularity which parts of Vitek she is relying on to supplement the noted deficiencies in Vitek's actual phagocytosis assay. However, for the reasons given above, it is submitted that the rejection should be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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